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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,863	05/01/2001	Philip Goelet	13020-2-D1	5388

7590 06/24/2005

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EXAMINER	
SISSON, BRADLEY L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/846,863	GOELET ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 06 May 2005 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 32-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

4. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in

the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

5. For convenience, claims 32, 39, and 56 the only independent claims, are reproduced below.

Claim 32 (currently amended): A method for identifying single nucleotide polymorphic sites in a genome of a species of interest, comprising:

(a) isolating a plurality of DNA fragments from the genome of a population of individual representatives of the species of interest, wherein each fragment corresponds to a location of the genome and the fragments are between about 0.1 kb and 10.0 kb;

(b) sequencing the DNA fragments to determine the nucleotide sequences of each fragment, and

(c) comparing the sequence of each fragment to corresponding fragments from other individual representatives of the species of interest to identify single nucleotide polymorphic sites ~~of sequence variation~~, wherein the species of interest is a mammal and the comparison is made among mammals of the same species.

Claim 39 (currently amended): A method for determining allelic frequency at a single nucleotide polymorphic site, comprising:

(a) isolating a plurality of DNA fragments from a population of two or more individual representatives of a species of interest, wherein each fragment corresponds to a location of the genome and the fragments are between about 0.1 kb and 10.0 kb;

(b) sequencing the DNA fragments to determine the nucleotide sequences of each fragment;

(c) comparing the sequence of each fragment to corresponding DNA fragments from different individual representatives of the species of interest and identifying single nucleotide polymorphic sites having at least two alleles, wherein the species of interest is a mammal of the same species and the comparison is made among mammals of the same species,

(d) determining the base identity of each allele present in the location of the genome, and

(e) calculating the allelic frequency for each allele by dividing the frequency at which each allele appears in the sample set by the total number of individuals ~~, wherein the species of interest is a mammal of the same species~~.

Claim 56 (new): A method of determining the likelihood that a horse is or is not an offspring of a putative parent, comprising:

a) isolating a plurality of DNA fragments from upper and lower strands of putative offspring horse genomic DNA, the upper and lower strands comprising single nucleotide polymorphic sites that each have an allelic frequency of at least 0.20;

b) isolating a plurality of DNA fragments from upper and lower strands of putative parental horse genomic DNA, the upper and lower strands comprising single nucleotide polymorphic sites that each have an allelic frequency of at least 0.20;

c) identifying the single nucleotide polymorphic sites of the putative parental genomic DNA and the putative offspring genomic DNA by determining the nucleotide base identity at each single nucleotide polymorphic site;

d) comparing single nucleotide polymorphic sites that match between the putative parental genomic DNA and the putative offspring genomic DNA, thereby determining the likelihood that the horse is or is not the offspring of the putative parent.

6. As presently worded, the method of claim 32 has been interpreted as encompassing the identification of an infinite number of single nucleotide polymorphisms in any and all regions of a genome of any mammal. Said method has also been interpreted as fairly encompassing the simultaneous detection and identification of any and all single nucleotide polymorphisms in any and all DNA fragments, where the DNA fragments represent the same, complete, or different segments of genomes of different subspecies and/or variants of any and al mammals. Said claims have also been interpreted as encompassing performing said determination when there does not exist any knowledge of any part of the nucleotide sequence of any or all of the fragments.

7. A review of the disclosure finds the following examples:

Page 45:

EXAMPLE 1
DISCOVERY OF EQUINE POLYMORPHISMS

Page 47:

EXAMPLE 2
CHARACTERIZATION OF EQUINE POLYMORPHISMS

Page 50:

EXAMPLE 3
ALLELIC FREQUENCY ANALYSIS OF EQUINE POLYMORPHISMS IN SMALL POPULATION STUDIES

Page 55:

EXAMPLE 4
PARENTAGE TESTING

Page 56:

EXAMPLE 5
IDENTITY TESTING

Page 58:

EXAMPLE 6
ANALYSIS OF A HUMAN SNP

8. Of the six examples provided, none disclose how one would test and evaluate the myriad "species of interest," much less identify said single nucleotide polymorphisms in a simultaneous manner any number of individuals (claims 32, 36-39, and 43-45), or when testing the "smaller" value of 10,000 individuals (limitation of claims 35 and 42).

9. While the specification does present several examples, such are directed to the analysis of but equine and human DNA and then primarily to the analysis of equine DNA as it relates to parentage analysis (Example 4). Said six examples do not provide an adequate written description of the claimed method whereby one would be able to determine any and all single nucleotide polymorphisms in any and all species of mammals. As presently worded, the claimed method fairly encompasses performing the identification when but one strand is sequenced and/or is present in but only one haploid example. Page 47 of the disclosure, however, teaches, "Differences were concluded to be a DNA polymorphism only if the data was available for both strands, and/or present in more than one haploid example among the five horses tested." The specification does not provide an adequate written description of how to practice the full scope of the invention where but one strand is analyzed and/or where the frequency of the polymorphism is less frequent than 1 in 5, be the species human, equine, or non-human primate, dogs, cats, cattle, or sheep, as is recited in claim 48 and 53.

10. Example 1 clearly teaches that equine polymorphisms were identified in the breed of horses known as thoroughbred. The specification has not provided any teaching that polymorphisms found in one breed is also found in another breed, especially when the phenotype

of the breeds is highly divergent, which in turn fairly suggests that the genetic makeup of the two equines is highly dissimilar, e.g., the Lithuanian Heavy Draft and the Noma, where the Lithuanian Heavy Draft was first recognized in 1964, with the Noma originating in the seventeenth century. While both are horses, the existence of one for centuries and the non-existence of the other until a few decades ago speaks to their genetic diversity. The specification fails to provide an adequate written description of how one would recognize and use single nucleotide polymorphisms (SNPs) in one breed to in turn recognize an individual in another breed, much less determine paternity.

11. Clearly, the limited disclosure provided by the specification does not constitute an adequate written description of the full genus of embodiments encompassed by the claims. Such limited disclosure also does not reasonably suggest that applicant was in possession of the claimed invention at the time of filing. Accordingly, and in the absence of convincing evidence to the contrary, Claims 32-58 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

12. Claims 32-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513

> (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

13. Of the six examples provided, none disclose how one would test and evaluate the myriad "species of interest," much less identify said single nucleotide polymorphisms in a simultaneous manner any number of individuals (claims 32, 36-39, and 43-45), or when testing the "smaller" value of 10,000 individuals (limitation of claims 35 and 42).

14. While the specification does present several examples, such are directed to the analysis of but equine and human DNA and then primarily to the analysis of equine DNA as it relates to parentage analysis (Example 4). Said six examples do not enable the identification of mutations in any and all mammalian species of interest.

15. As presently worded, the method of claims 32-47, 49, and 50 fairly encompasses the analysis of virtually any mammal. And in the case of claims 32 and 40, virtually an infinite number of individuals can be tested simultaneously and that the reaction comprises DNA

fragments from the entire genome of an infinite number of individuals from an infinite number of species of mammals. The six examples provided do not set forth a reproducible procedure whereby one of ski in the art would be able to correctly associate a potential polymorphism with a given sequence when similar sequences are present yet belong to a different species of mammal. Assuming *arguendo* that one of skill in the art would have been able to identify SNPs in any genetic materials found in any "species of interest," a position that the Office does not concede, such is not enough to enable the claimed method in that the specification must also enable the use of the SNPs. As shown above, the claims method is considered to encompass the identification of SNPs in any "species of interest" where said species of interest encompasses all life forms as well as all viruses. The method clearly encompassing mutations that are silent as well as non-silent, yet the specification is effectively silent as to how one is to use such mutations in any mammalian species of interest.

16. A claim 46 requires one to use the polymorphism to identify the mammal. The specification does not provide the requisite starting materials, e.g., the polymorphisms that are species specific, much less teach a reproducible procedure where any one of said polymorphisms is used to identify the species. Similarly, the specification fails to set forth a reproducible procedure whereby any human, non-human primate, dog, cat, sheep, cattle or horse would be identified, much less determine the parentage of same

17. In view of the breadth of scope of the claims, the introduction of new matter into the disclosure, the limited disclosure provided, the unpredictability in the art, claims 32-58 are not enabled by the disclosure. Accordingly, and in the absence of convincing evidence to the

contrary, claims 32-58 are rejected under 35 USC, 112, first paragraph, as not being enabled by the disclosure.

Response to argument

18. At pages 12-27 applicant's representative presents argument that the specification is enabling and does provide an adequate written description, asserting, "that genomic DNA is genomic DNA regardless of the species. This DNA does not chemically vary between species..." Supporting this argument is a showing of BLAST search results for SEQ ID Nos.: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 25, 45, and 71.

19. The above argument has been fully considered and has not been found persuasive. Clearly, DNA varies between species as it varies within a species for if there was absolutely no difference in the DNA of the cells, then all life forms would be identical, which clearly they are not. Indeed, not all humans look the same, which is a direct result of there being differences in their genomic DNA.

20. While applicant's representative has provided sequence comparisons, it is less than clear if these sequences are found in the same gene(s), and more particularly, the showing is completely silent as to there being a SNP associated with this sequence in each of the life forms, and that if present, the SNP is useful in identifying the species, and/or the parents of the individual.

21. At page 27 of the response said representative provides opinion argument as to what one of skill in the art would have understood. This argument has been fully considered and has not been found persuasive. Attention is directed to MPEP 2145.

> Attorney argument is not evidence unless it is an admission, in which case, an examiner may use the admission in making a rejection. See MPEP § 2129 and § 2144.03 for a discussion of admissions as prior art.
> The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness."). See MPEP § 716.01(c) for examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration.

22. At page 28 of the response applicant's representative asserts that the claimed method is distinguishable over *Genentech,* as the claims are not drawn to cleaving a protein, which was the novel aspect of the invention. Said representative asserts "the novel aspect of the amended claims does not include claims to individual SNPs, but method using the combinations of SNPs as useful genetic markers."

23. The above argument has not been found persuasive for while agreement is reached in that some of the claims are drawn to a method of using SNPs as genetic markers (to identify any mammal (claim 46); to determine the parentage of any mammal (claim 47)), the specification, like that of *Genentech*, does not provide the requisite starting materials (SNPs that enable the full genus of mammalian species, and identify the parents f any offspring, be if dog, cat, sheep, cow, horse, etc.). Absent such essential materials, one is forced to resort to trial and error testing in an attempt to identify the species or parent. While said representative has presented a showing of how numerous sequences are found in different, divergent organisms, such speaks to the inability of these sequences to differentiate between a Norway rat, a house mouse, a chimpanzee, a human, a cow, etc. Furthermore, and as described above, there is no showing that these conserved sequences contain a SNP in each instance, much less a showing that the SNP is useful.

24. For the above reasons, and in the absence of convincing evidence to the contrary, claims 32-58 are rejected under 35 USC, 112, first paragraph, as not being enabled by the disclosure.

Conclusion

25. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

a. Breeds of Livestock, "Noma," from webpage www.ansi.okstate.edu/breeds/horses/noma/index.htm; print date 22 June 2005;

b. Breeds of Livestock, "Lithuanian Heavy Draft ," from webpage www.ansi.okstate.edu/breeds/horses/lithuanianheavydraft/index.htm; print date 22 June 2005.

27. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

28. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

31. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
22 June 2005